REMARKS

The final Office Action of September 15, 2009 and the prior art relied upon therein have been carefully studied. Favorable reconsideration and allowance of the claims are requested.

I. Claim Status and Amendments

Claims 2-3 and 6-14 were pending in this application when last examined and stand rejected. No claims have been allowed.

By way of the present amendment, claim 11 has been amended to correct a typographical error and new claims 15-18 have been added. New claims 15-16 correspond to the compound of claim 2 and to the treatment aspect of claims 7-8. New claims 17-18 correspond to the compound of claim 3 and to the treatment aspect of claims 13-14. Further support can be found throughout the disclosure. No new matter has been added.

It is respectively submitted that this amendment should be entered and considered, even though the case is after final rejection, because it should not raise new issues or require a new search. The examiner has already considered the treatment aspect of newly added claims 15-18. In this regard, the examiner, in item 5 on page 2 of the Office

Action, has already considered and acknowledged that the specification enables and supports the treatment aspect of the newly added claims. Thus, new claims 15-18 simply correspond to the subject matter indicated as enabled by the examiner in the last Office Action. For this reason, it is believed that the claims should not raise any new issues requiring further examination or search.

Claims 7-8 and 13-14 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

Claims 2, 3 and 9-12, and 15-18 are pending upon entry of this amendment. These claims define patentable subject matter warranting their allowance for the reasons set forth herein.

II. Enablement Rejection

Claims 13-14 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement for the reasons in item 5 on pages 2-4 of the Action. The examiner states that the specification is enabling for treatment, but for not prevention.

Applicants respectfully disagree. Nonetheless, for the sole purpose of expediting prosecution and not to

acquiesce to the rejection, Applicants have removed the "prevention" aspect from the claims. It should be noted that new claims 15-18 refer only to treatment. Indeed, the new claims correspond to the subject matter indicated as enabled by the examiner in item 5 on page 2 of the Office Action. Withdrawal of the rejection is requested.

III. Objection the Claims

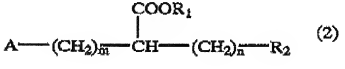
In item 6 on page 4, the examiner objects to claims 7-8 and 13-14 as being improper dependent claims for failing to further limit the subject matter of the claims to which they depend. The examiner states that the intended uses, recited therein, do not further limit the scope of the claims. Without acquiescing to the examiner's position, the present amendment hereby renders the objection moot for reasons by cancelling the objected claims. Again, new claims 15-18 correspond to the treatment aspect of the previous claims 7-8 and 13-14. Withdrawal of the rejection is requested.

IV. Obviousness Rejection

Claims 2, 3, and 6-14 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jo et al. (WO 0142186 (see English translation US 6,737,417) for the reasons in item 8 on pages 5-8 of the Office Action. This rejection

is respectfully traversed for the reasons set forth in the response filed June 4, 2009, which arguments are reiterated herein by reference, and for the following reasons.

First, at page 5 of the Office Action, the examiner states that Jo et al. teaches a genus that encompasses the claimed compound, and the only difference between the prior art compounds and the claimed compounds are the substituents at the 17-position. At page 6, the examiner further states that Jo et al. teaches 17-substitutents inclusive of the claimed compounds. However, it should further be noted that Jo et al. discloses a compound by indicating a general formula (2) as follows:



(2)

In the formula, A is selected from formulas (3) to (26), some of which have further variation of substituents. See columns 4-8 of Jo et al. Thus, in contrast to the examiner's position, Jo et al. discloses a huge number of compounds within a genus but does not disclose any specific compound having a 17-substitutent, inclusive of the claimed compounds.

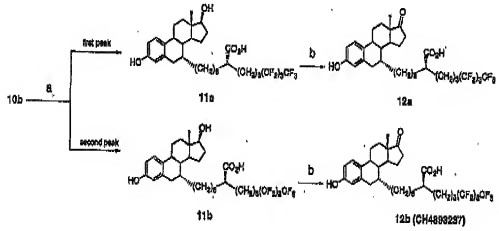
Second, at page 7 of the Office Action, the examiner argues that the data in the specification does not support

Applicants' previous arguments with respect to unexpected results. In particular, regarding Table 2 of the specification, the examiner states that "(a) compound 1 has a higher AUC value than control compounds 1 and 2 but a lower or equal AUC value compared to control compound 2 and (b) compound 4 has a lower AUC value than control compounds 1 and 2." Applicants disagree.

Regarding Compounds 1 and 4, the present specification also discloses Table 3 that shows AUC values in cynomolgus monkeys. In Table 3, AUC values for compounds 1 and 4 are 2.42 and 3.8, respectively. These values are significantly high than that for Control Compound 1 (0.42). Therefore, the data in Table 3 indicates that the claimed compounds exhibit significantly high bioavailability in monkeys, which belong to a primate, such as humans.

In this connection, Applicants are enclosing herewith a copy of a reference to Kanbe et al. (Bioorganic & Medicinal Chemistry Letters, 16 (2006), pp. 4959-4964), in which the present inventors of Yoshiaki Nabuchi, Hiroshi Araya, Setsu Kawata, Kazumi Morikawa, Yoshitake Kanbe, Yoshihito Ohtake, Shinichi Kaiho, Kenji Taniguchi and Toshiaki Tsunenari are listed as co-authors. The Kanbe et al. reference discusses the results of the same pharmacokinetic assay in more detail.

In particular, the Kanbe et al. reference discloses Compounds 11a, 11b and 12b, which were prepared in the following procedure. In the procedure, the chiral resolution of compound 10b gives Compounds 11a and 11b in a first peak and a second peak, respectively. Compound 12b was obtained by oxidation of Compound 11b. These procedures are identical to the procedures in Example 1 of the instant application, and therefore Compounds 11a, 11b and 12b in the reference correspond to Control Compound 2, Control Compound 1, and Compound 1 in the subject specification, respectively.



The Kanbe et al. reference discloses the pharmacokinetic data of these compounds in Table 4 as follows:

Table 4. Pharmacokinetic data of rats, mice, and monkeys

Compound	Animal species	AUC, po (μg h/mL)			AUC, iv (μg h/mL)		Bioavailability (%)
		Dose (mg/kg)	Intact	17-metabolite (compound)	Dose (mg/kg)	Intact	
11a	Rat	20[a]	190	n.d.[e] (12a)	10[a]	254	37
	Mouse	30[b]	470	297 (12a)	10[d]	447	35
	Monkey	3[c]	0.30	6.66 (12a)	N.D.[f]	N.D.[f]	N.D.[f]
11b	Rat	20[a]	98	n.d.[e] (12b)	10[a]	146	34
	Mouse	30[b]	274	194 (12b)	10[d]	264	37
	Monkey	3[c]	0.42	3.20 (12b)	3[c]	88	0.48
12b (CH4891237)	Rat	20[a]	32	n.d.[e] (11b)	10[a]	50	32
	Mouse	30[b]	468	37 (11b)	10[d]	389	40
	Monkey	3[c]	2.42	0.19 (11b)	3[c]	77	3.1

[a] Compound dosed in Sprague-Dawley rats as a solution in water/PEG200/EtOH (3:6:1).
[b] Compound dosed in CD-1 mice as a suspension in 5% gum arabic.
[c] Compound dosed in cynomolgus monkeys as a solution in water/PEG200/EtOH (4:3:3).
[d] Compound dosed in CD-1 mice as a solution in water/PEG200/EtOH (3:6:1).
[e] n.d., not detected.
[f] N.D., no data.

In the table, the values of AUC of mice, i.e. Compound 11a: 470, Compound 11b: 274, Compound 12bl 468, correspond to the data in Table 2, i.e. Control Compound 2, Control Compound 1, and Compound 1, respectively, as disclosed in the present specification. On the other hand, this table also shows AUC values in monkey, Compound 11a: 0.30, Compound 11b: 0.42, Compound 12b: 2.42.

As can be seen, the claimed compounds, as represented by Compound 12b, have a higher and more potent pharmacological efficacy in oral administration, as compared to Control Compounds 1 and 2, which correspond to the compounds of Jo et al. Based on such, Applicants respectfully submit that the experimental results in the subject specification (as confirmed by the data in Kanbe et al.) clearly demonstrate that the compounds within the entire scope

of the amended claims have a superior and beneficial effect over anything that could be expected from the teachings in the prior art. Again, Jo et al. fails to include any teaching or suggestion regarding such excellent pharmacokinetic properties of the subject invention.

In view of the above, it should be clear that the claimed compounds differ structurally and in chemical properties from the compounds in Jo et al., and it is believed that the above-noted results constitute unexpected results indicative of the non-obviousness of the claims, since they show that compounds of the claims exhibit superior effects and properties over the compounds in Jo et al. In this regard, it is well established that the presence of unexpectedly improved properties or properties not present in the prior art are indicative of non-obviousness. *Dillon*, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990). *See also* M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 716.02(a) I-IV and § 2145.

In view of above, it is believed that one of ordinary skill in the art could not conceive of the claimed invention even in light of the disclosure of Jo et al. and therefore the rejection should be withdrawn.

In addition, at page 6 of the Office Action, the examiner states in the Office Action that "Applicant also

argues the instant claims are optically active whereas the compounds of Jo et al. are diastereomer mixtures". In reply, it should first be made very clear that the claimed invention is not limited only to covering optical active compounds, and second Applicants did not make such an argument in the last response. Instead, in the last response, Applicants simply pointed out that Compounds 1 and 2 are optically active compounds of the claimed invention and were prepared in Example 2 (pages 19-20) of the subject specification from Control Compounds 1 and 2, respectively. Jo et al. do not disclose or suggest these compounds. Instead, Jo et al. disclose the diastereomer mixture of Control Compounds 1 and 2 in Example 15 (column 94 of US 6,737,417 B2). It was further pointed out that Control Compounds 1 and 2 differ in chemical structure from Compounds 1 and 2 of the claims.

Applicants respectfully submit that the experimental data stated above, which was obtained by using optical active compounds of the claimed invention, fully covers the scope of the claimed invention.

For these reasons, it is believed that the compounds in Jo et al. are not the same as, nor are they suggestive of, the compounds of claims 2, 3, 9, and 11, and new claims 15-18; and the claimed compounds achieve unexpectedly improved properties indicative of non-obviousness. For these reasons,

the teachings of Jo et al. cannot render obvious the compounds of independent claims 2, 3, 9, and 11 and new claims 15-18. Thus, these claims and all claims dependent thereon are believed to be novel and patentable over Jo et al. Withdrawal of the above 103(a) obviousness rejection is therefore solicited.

V. Conclusion

Having addressed all the outstanding issues, the amendment is believed to be fully responsive to the Office Action. It is respectfully submitted that the application is in condition for allowance and notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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APPENDIX:

Attachments:

Kanbe et al. (Bioorganic & Medicinal Chemistry Letters, 16 (2006), pp. 4959-4964).